UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE	CONFIRMATION NO.
09/292,053	04/14/1999	MICHELLE REID	01272.0090	3037

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ART UNIT	PAPER NUMBER
1	25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/292,053	MICHELLE E. REFF	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

1. Claims 38-54 are pending.

2. In view of the amendment filed 10/30/02, the following objection and rejections remain.

3. The disclosure stands objected to under 37 CFR 1.821(d) because SEQ ID NO: is required on pages 50-52, 54-56, 59-60 and 62-63, including all sequences listed in Tables 1-5, pages 66-68; Appropriate correction is required.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 38-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of inhibiting IgE in a human subject in need of such inhibition comprising administering an IgE inhibiting effective amount of any ant-human CD23 antibody comprising a human gamma-1 constant region wherein the antibody human CD23 monoclonal antibody comprises *any* "primate antigen binding portion", or *any* "rodent antigen binding portion", (2) a method of inhibiting IgE in a patient in need of such inhibition comprising administering an IgE inhibiting effective amount of an anti-human CD23 antibody comprising *any* **human gamma constant region** wherein the anti-human CD23 antibody comprises a variable heavy domain having a sequence selected from the group consisting of the polypeptide of SEQ ID NO: 4 and SEQ ID NO: 8 encoded by a nucleic acid sequence of SEQ ID NO: 3 and 7; and a variable light domain having a sequence selected from the group consisting of the polypeptide of SEQ ID NO: 2 and SEQ ID NO: 6 encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and 5 for treating an IgE-mediated allergic disorder, (2) a method of inhibiting-IgE in a subject in need of such inhibition comprising administering an IgE-inhibitory effective amount of an anti-

human CD23 antibody comprising *any* human gamma constant region wherein the anti-human CD23 monoclonal antibody comprises *any* primate antigen-binding region or any rodent antigen-binding region for treating an IgE-mediated allergic disorder. (3) a method of inhibiting-IgE in a subject in need of such inhibition comprising administering an IgE- inhibitory effective amount of any anti-humnaCD23 antibody comprising any human gamma constant region wherein the anti-human CD23 monoclonal antibody comprises any "primate antigen-binding region" or any "rodent antigen-binding region" for treating an IgE-mediated allergic disorder such as allergic rhinitis, allergic contact dermatitis, anaphylactic reactions, asthma, and bronchitis, (4) the said method wherein the antibody is administered parenterally or wherein parentally includes subcutaneous, intravascular, intravenous, rectal, vaginal, and intraperitoneal administration, and (5) the said method wherein the antibody is lyophilized for storage and reconstituted prior to administration.

The specification discloses only a method of making various chimeric primate anti-human CD23 antibodies such as 5E8 and 6G5 containing only a human gamma 1 constant region and the antigen binding portion of said antibody from primate or rodent wherein the anti-human CD23 antibody comprises a variable heavy domain having a sequence selected from the group consisting of the polypeptide of SEQ ID NO: 4 and SEQ ID NO: 8 encoded by a nucleic acid sequence of SEQ ID NO: 3 and 7; and a variable light domain having a sequence selected from the group consisting of the polypeptide of SEQ ID NO: 2 and SEQ ID NO: 6 encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and 5 for a method of inhibiting IgE-mediated allergic disorder such as allergic rhinitis, allergic contact dermatitis, anaphylactic reactions, asthma, and bronchitis.

Other than the specific anti-CD23 antibody comprising the specific gamma 1 constant region, and the specific antigen-binding region from primate or rodent, there is insufficient written description about the structure associated with function of any "primate antigen-binding portion or "rodent antigen-binding portion". The term "primate antigen-binding portion" or "rodent antigen-binding portion" does not convey the specific structure, much less about the function. Note, one skill in the art would recognize the "antigen-binding portion" is referring to the antigen binding portion or the Fab fragment of the CD23 antibody with antibody specificity to the antigen CD23. The claims as written encompassed *any* anti-human CD23 monoclonal antibody and any primate antigen binding portion or any rodent antigen binding portion where the

antigen binding portion binds to primate or rodent, which is quite different from the human CD23 as the antigen to which the antibody binds.

Further, the specification discloses only two chimeric anti-human CD23 antibodies such as 5E8 and 6G5 containing only human gamma 1 constant region for a method of inhibiting IgE-mediated allergic disease. Given the lack of a written description of *any* additional representative species of chimeric human CD23 antibody that contains other gamma constant region, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 39, 41 and 49-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a primate antigen-binding portion or region" in claims 39 and 49 is indefinite and ambiguous because a single amino acid would still be considered a portion and it is not clear which primate antigen binding portion is being claimed. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed limitation.

The recitation of "a rodent antigen-binding portion or region" in claims 41 and 49 is indefinite and ambiguous because a single amino acid would still be considered a portion and it is not clear which primate antigen binding portion is being claimed. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed limitation. It is suggested that the claims be amended to recite wherein the anti-human CD23 monoclonal antibody comprises an antigen-binding portion from primate or rodent.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 38, 40-45, 47 and 49-50 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO 96/12741 publication (of record, May 1996, PTO 1449) as evidence by Saxon et al (of record, J Immunol 147(11): 4000-4006, 1991; PTO 1449).

The WO 96/12741 publication teaches a method of inhibiting IgE in a patient such as rat or monkeys (page 31, Example 12, in particular) comprising administering a pharmaceutical effective amount of monoclonal anti anti-CD 23 antibody or humanized antibody that contains a rodent binding portion and a human gamma 1 constant region (See claims 20 and 11-15, page 4, lines 1-3, and lines 15-19, lines in particular). The reference anti-CD23 antibody inhibits IgE production in vivo and IgE mediated B cell differentiation in vivo (See page 8, line 25-28, claims 1-4 in particular). Further, the WO 96/12741 publication teaches a method of inhibiting allergy such as asthma and bronchitis, rhinitis in a patient using chimeric and humanized anti-CD23 antibody and the reference humanized antibody contains IgG 1 constant region (See claims 20, 8 and 11-15, page 4, lines 1-3, and lines 15-19, lines in particular). It is an inherent property of anti-CD23 antibodies to inhibit IgE expression induced by IL-4 as evidence by Saxon et al (See abstract, and page 4004, column 1, in particular). Claim 43 is included in this rejection because the ability of the reference anti-CD23 antibody to inhibit IgE expression in vivo is an inherent property and the anti-CD23 would also inhibit the IgE expression in vitro. Thus, the reference teachings anticipate the claimed invention.

Applicant's arguments in the amendment filed 10/30/02 have been fully considered but are not persuasive.

Applicants' position is that (1) the WO 96/12741 does not anticipate the claimed method given the potential antagonists are anti-human CD23 antibodies which may comprise different type of human constant and other species domains including human gamma1, gamma 2, gamma 3 and gamma 4. (2) no anti-human CD23 antibodies are exemplified which comprises a human constant domain, much less a human gamma constant domain. (3) there is no specific teachings relating to the administration of an anti-human CD23 IgG1 antibody to inhibit IgE in a patient in

need of such inhibition unless different teachings of the reference are combined and chosen in lieu of other teachings.

However, the WO 96/12741 publication teaches a method of treating allergic disease comprising administering a pharmaceutically effective amount of a binding agent to CD23 such as humanized or chimerized CD23 antibody where the reference antibody may be a human IgG constant domain such as IgG1 (See page 5, lines 26, claims 13-14 and 20 of WO 96/12741 publication). The reference antibody blocks the interaction between CD23 and a ligand which binds to it (See page 3, lines 25-26, in particular). Even without the Saxon et al reference, the WO 96/12741 publication still teaches that the reference anti-CD23 antibody inhibits IgE production and IgE mediated B cell differentiation in vivo (See page 8, line 25-28, claims 1-4 in particular). Note, this rejection can be overcome by amending the claims to recite a specific SEQ ID NO.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 38-39, 43, 49 and 51-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 96/12741 publication (of record, May 1996, PTO 1449) in view of Saxon et al (of record, J Immunol 147(11): 400-4006, 1991; PTO 1449) and US Pat No. 5,658,570 (of record, Aug 1997, PTO 892).

The teachings of the WO 96 12741 publication have been discussed supra.

The claimed invention as recited in claim 39 differs from the reference only that the anti-human CD 23 monoclonal antibody comprises a primate antigen-binding portion.

The claimed invention as recited in claim 43 differs from the reference only that the anti-human CD23 monoclonal antibody inhibits IgE expression in vitro.

The claimed invention as recited in claim 51 differs from the reference only that the anti-human CD23 monoclonal antibody is administered parenterally.

The claimed invention as recited in claim 52 differs from the reference only that the anti-human CD23 monoclonal antibody is administered parenterally wherein parenterally includes subcutaneous, intravenous, rectal, vaginal, and intraperitoneal administration.

The claimed invention as recited in claim 53 differs from the reference only that the anti-human CD23 monoclonal antibody is administered by subcutaneous administration.

The claimed invention as recited in claim 54 differs from the reference only that the anti-human CD23 monoclonal antibody is lyophilized for storage and reconstituted prior to administration.

The '570 patent teaches chimeric or humanized anti-CD23 antibodies which comprise a human constant region of IgG isotype and a primate antigen binding region (See claims 1-8, and column 8, lines 52-53) and a method of administering a therapeutically amount of said antibodies (See column 6, lines 1-8, in particular). The '570 patent teaches the antibody constant region derived from a human to ensure that they appear more human-like so that the probability of adverse reaction is lessened (See column 5, lines 32-38, in particular). The '570 patent teaches the reference human CD23 antibody is useful for parenteral administration such as subcutaneously, intramuscularly, intravenously, orally, rectally, vaginally, and intraperitoneally (See column 22, lines 22-28, column 25, lines 20-23, in particular). The '570 patent further teaches the reference antibody can be lyophilized for storage and reconstituted in a suitable carrier prior to use (See column 26, lines 8-10, in particular). The '570 patent teaches the reference antibody human constant region can be any desired isotype (See column 37, claim 21, in particular) such as human gamma 1 (See claim 38 of '570, in particular).

Saxon *et al* teach anti-CD23 antibodies inhibit IgE expression (See abstract, page 4002, column 2, Suppression of ongoing IgE production by FcεII (CD23) mab, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti-CD23 antibody as taught by the WO 96/12741 publication for the anti-human CD23 monoclonal antibody comprises a primate antigen binding

portion and human constant IgG1 as taught by The '570 patent for a method of inhibiting IgE mediated allergy in a human subject as taught by the WO 96/12741 publication and Saxon *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '570 patent teaches the antibody constant region derived from a human would ensure that the antibody appears more human-like so that the probability of adverse reaction is lessened (See column 5, lines 32-38, in particular). The WO 96/12741 publication teaches chimeric humanized anti-CD 23 antibody is useful for inhibiting IgE production and IgE mediated B cell differentiation in vivo for a method of treating IgE mediated allergic disorders (See claims 20 and 11-15, page 4, lines 1-3, and lines 15-19, lines in particular). Saxon *et al* teach anti-CD23 antibodies inhibit IgE expression (See abstract, page 4002, column 2, Suppression of ongoing IgE production by FcεII (CD23) mab, in particular).

Applicant's arguments in the amendment filed 10/30/02 have been fully considered but are not persuasive.

Applicants' position is that (1) the WO 96/12741 does not anticipate the claimed method given the potential antagonists are anti-human CD23 antibodies which may comprise different type of human constant and other species domains including human gamma1, gamma 2, gamma 3 and gamma 4. (2) No anti-human CD23 antibodies are exemplified, which comprises a human constant domain, much less a human gamma constant domain. (3) There is no specific teachings relating to the administration of an anti-human CD23 IgG1 antibody to inhibit IgE in a patient in need of such inhibition unless different teachings of the reference are combined and chosen in lieu of other teachings. (3) The Saxon reference antibodies may inhibit IgE production, however the reference does not teach or suggest at the date of invention that the subject IgG1 anti-human CD23 antibodies would possess advantageous properties vis-à-vis other types of anti-human CD23 antibodies such that one skilled in the art would have motivated to select such antibody for therapy. (4) The '570 patent is again cited based on its disclosure relating to the production of primatized antibodies. However, the '570 does not teach the enhanced IgE inhibiting properties of primatized anti-CD23 antibodies possessing human gamma 1 constant domain.

However, the WO 96/12741 publication teaches a method of treating allergic disease comprising administering a pharmaceutically effective amount of a binding agent to CD23 such as humanized or chimerized CD23 antibody where the reference antibody may be a human IgG

constant domain such as IgG1 (See page 5, lines 26, claims 13-14 and 20 of WO 96/12741 publication). The reference antibody blocks the interaction between CD23 and a ligand, which binds to it (See page 3, lines 25-26, in particular). Even without the Saxon et al reference, the WO 96/12741 publication still teaches that the reference anti-CD23 antibody inhibits IgE production and IgE mediated B cell differentiation in vivo (See page 8, line 25-28, claims 1-4 in particular).

In response to applicants' argument that the none of the reference teach human gamma 1 constant region, the WO 96/12741 publication teaches a method of treating allergic disease comprising administering a pharmaceutically effective amount of a binding agent to CD23 such as humanized or chimerized CD23 antibody where the reference antibody may be a human IgG constant domain such as IgG1 (See page 5, lines 26, claims 13-14 and 20 of WO 96/12741 publication). Further, the '570 patent teaches the reference antibody human constant region can be any desired isotype (See column 37, claim 21 of the '570 patent, in particular) such as human gamma 1 (See claim 38 of '570, in particular).

In response to applicants' argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., enhanced IgE inhibiting properties) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

13. The following new ground of rejection is necessitated by the amendment filed 10/30/02.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claim 52 is rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The "intravascular" in claim 52 represents a departure from the specification and the claims as originally filed because said "intravascular" has no support in the specification and the

claims as originally filed. Further, Applicants have not pointed out the support for said "intravascular" comes from.

16. Claims 46 and 48 are free of prior art.

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
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January 13, 2003

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